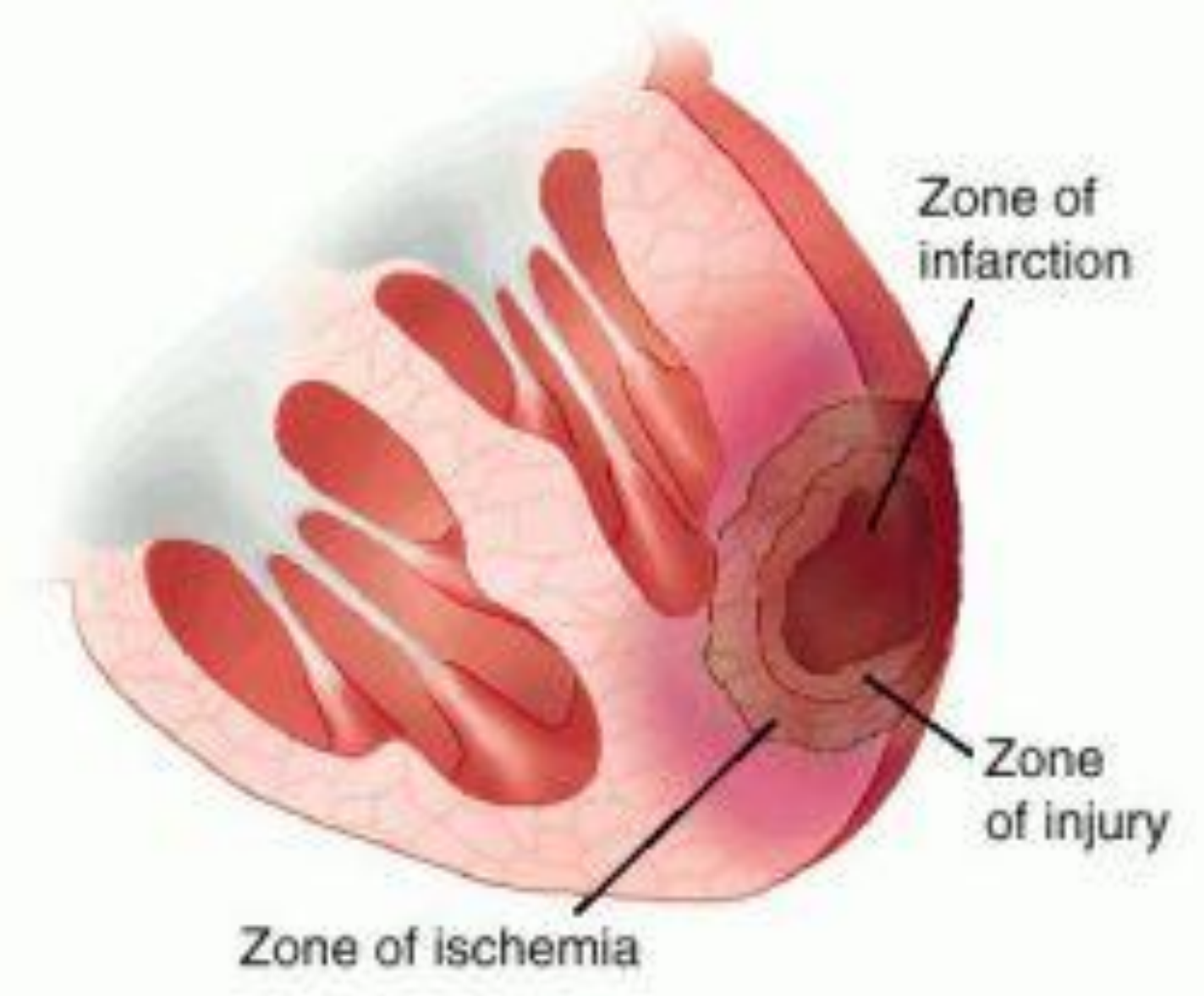
6^{th} Lecture

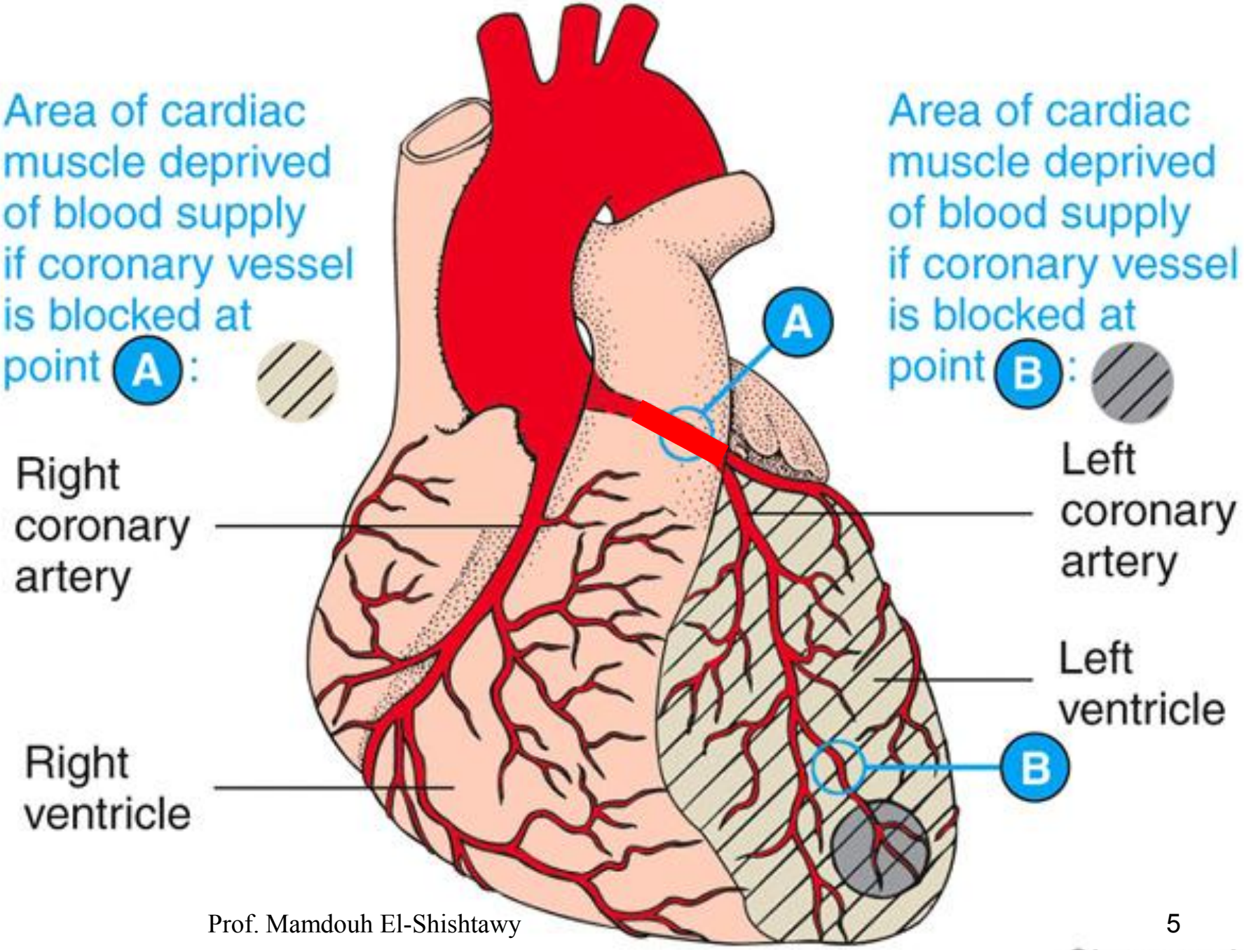
Myocardial Infarction

(Myocardial ischemia, Coronary thrombosis, or Heart attack)

Myocardial Infarction

- Myocardial Infarction (MI) is the interruption of blood supply to part of the heart muscle (myocardium), causing heart cells to die (necrosis). This is most commonly due to occlusion (blockage) of a coronary artery.


Zone of
infarction
Zone
of injury
Zone of ischemia


Area of cardiac muscle deprived of blood supply if coronary vessel is blocked at point A:
Area of cardiac muscle deprived of blood supply if coronary vessel is blocked at point B:
A
B
Right coronary artery
Left coronary artery
Left ventricle
Right ventricle

Angina Pectoris

- Angina pectoris, commonly known as angina, is severe chest pain due to ischemia (a lack of blood and hence oxygen supply due to obstruction or spasm of the coronary arteries) of the heart muscle,
- Coronary artery disease, the main cause of angina which is due to atherosclerosis.

Myocardial Ischemia & Time Factor

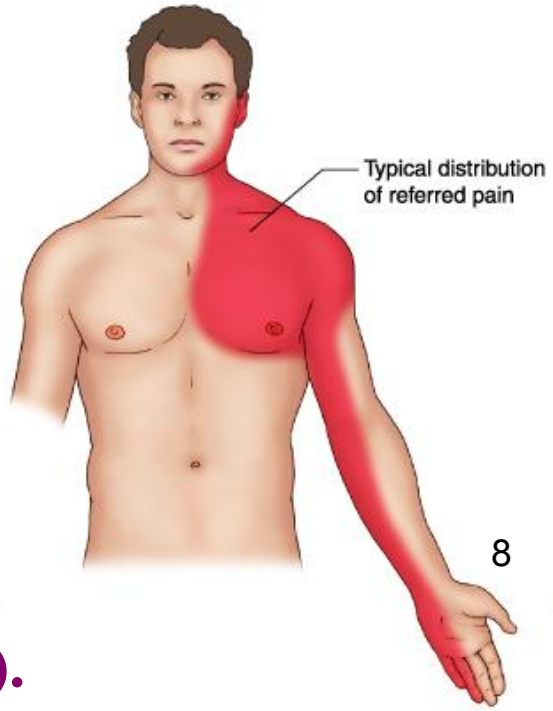
- The earlier the treatment is begun, the better the prognosis.

Myocardial infarction

- **Myocardial infarction (MI)** or **acute myocardial infarction (AMI)**, commonly known as a **heart attack**

- Typical symptoms of acute myocardial infarction:

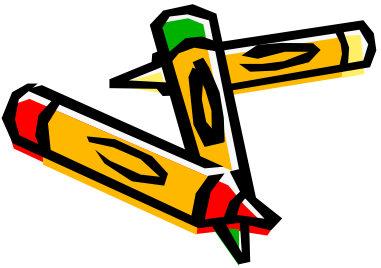
1. Chest pain (typically radiating to the left arm or left side of the neck)
2. shortness of breath **(dyspnea)**
3. Nausea
4. Vomiting
5. Palpitations
6. Sweating
7. Anxiety
8. Fatigue



9. **Often feels the death is imminent (وشيك).**

Typical signs of MI are:

1. Tachycardia.
2. A barely perceptible pulse (نبض لا يكاد يلمس),
3. Low blood pressure and
4. Elevated temperature.



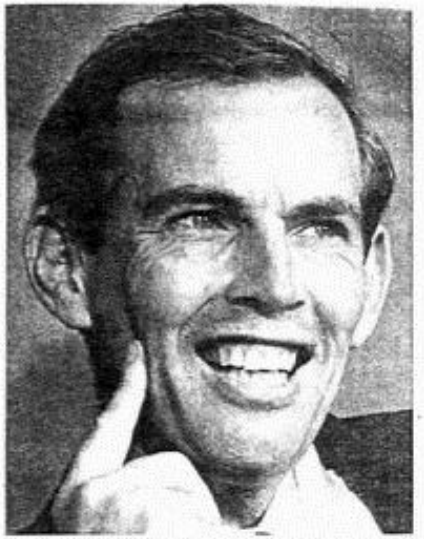
Myocardial Infarction (MI)

- **Note:** Approximately one fourth of all myocardial infarctions are silent, without chest pain or other symptoms. These cases can be discovered later on ECGs, or using blood enzyme tests.
- A silent course is more common in:
  1. Elderly,
  2. Patients with diabetes mellitus,
  3. After heart transplantation, probably because the donor heart is not connected to nerves of the host.

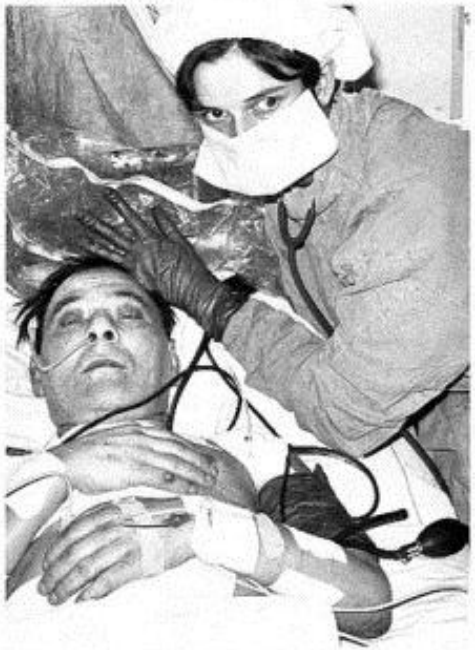
Moments in History

In December, 1967, a young woman, Denise Darvall, was walking across a street in Woodstock to buy a cake when a car struck her. She died in Groote Schuur Hospital and in doing so achieved immortality by becoming the world's first heart donor when Christiaan Neethling Barnard transferred her heart into the chest of Louis Washkansky.

Cape Town has been witness to many historic moments since the day Van Riebeeck anchored in Table Bay. Few, if any, brought more limelight to the city than the heart transplant. For the surgeon, Dr Barnard, soon to be a household name throughout the world, "the heart is merely a pump". But for those who equated the heart with love and death, the transplant seemed close to a miracle.



Professor Chris Barnard, leader of the heart-transplant team, in a characteristic pose during one of his many press conferences.



First close-up photograph to be taken of Mr Louis Washkansky, who underwent the world's first heart-transplant operation, was taken by a surgeon using an *Argus* photographer's camera at Groote Schuur Hospital. Mr Washkansky, whose condition was given as good, is being assisted to breathe by a respirator. 4.12.1967

"Mr Louis Washkansky, the 55-year-old Cape Town man whose life is being sustained today by the heart of a dead 25-year-old woman after the world's first successful heart transplant yesterday, is conscious in Groote Schuur Hospital and in a satisfactory condition." Monday, 4th December 1967

Diagnosis

- Diagnosis is often well indicated by patient history & ECG changes.
- However, the characteristic ECG pattern may not be present for up to 24 hr after the infarction.
- The changes from a normal ECG to an uncomplicated infarction pattern vary with:
  1. The site.
  2. The degree.
  3. the area of damage.

Diagnosis

- The development of cardiac arrhythmias, which is influenced by the site as well as the size of the infarction, is a major determinant of death in these patients.

Diagnosis

- A new infarction in a previously damaged heart will give an ECG pattern which is more difficult to interpret.
- Note: An ECG still remains the most specific diagnostic tool in evaluating the patient with chest pain.
- However, the initial ECG may be negative or non-diagnostic in > 40% of MI cases.

Cardiac Markers

- Cardiac markers are biomarkers measured to evaluate heart function.
- Most of the early markers identified were enzymes, and as a result, the term "cardiac enzymes" is sometimes used.
- However, not all of the markers currently used are enzymes.

Cardiac Markers

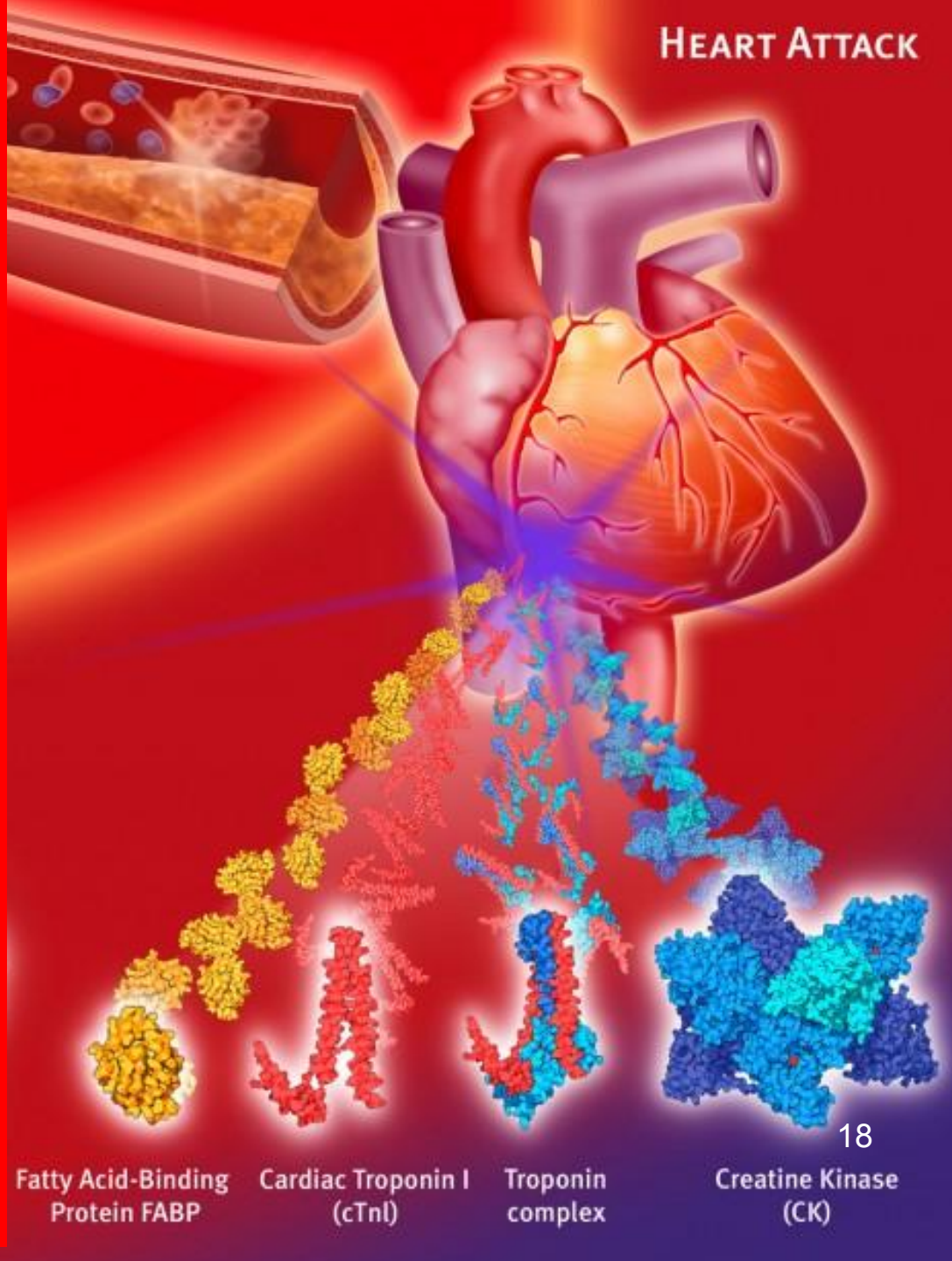
- Until the 1980s, the enzymes AST and LDH were used to assess cardiac injury.
- Now, cardiac markers include:
  1. Enzymes,
  2. Isoenzymes,
  3. Proteins.
- The cardiac markers leak out of injured myocardial cells through the damaged cell membranes into the bloodstream.

Cardiac Markers

- Biochemical markers are:

1. Enzymes (Aspartate aminotransferase (AST)).
2. Isoenzymes (Creatine kinase 2 (CK_2) (CK_{MB}) & Lactate dehydrogenase 1 (LDH_1) (H_4).
3. Proteins {Troponins, Myoglobin (Mb) & Fatty Acid Binding Proteins (FABP)}.

Release of fatty acid binding protein (FABP), myoglobin (Mb), CK_{MB} and cardiac troponins from the injured heart into plasma after AMI



Cardiac Markers

- Creatine kinase (CK) activities rise rapidly while AST & LDH1 show slower rise.
- Note that in the first 4 hours after the infarction the enzymes may not be raised.

CREATINE KINASE 1

- CK is a dimeric enzyme that regulates high energy phosphate production and utilization in contractile tissues.

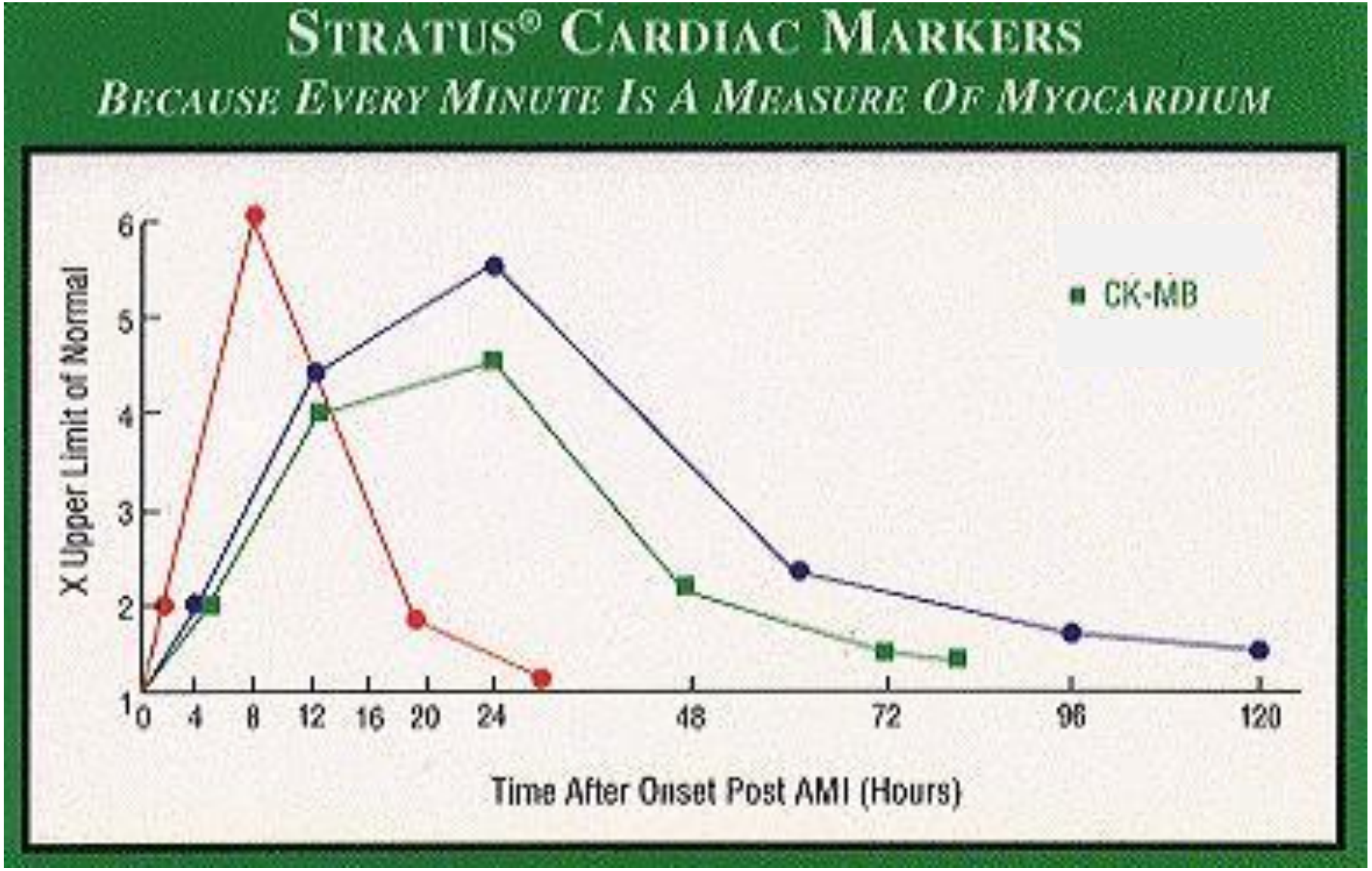
- There are different isoenzymes:
- CK1 (CK-BB): the predominant isoenzyme found in brain.
- CK2 (CK-MB): represent 20 – 30 % of total CK in diseased cardiac tissue
- CK3 (CK-MM): 98% in skeletal muscles and 1% in cardiac muscles.

1 Serum Creatine kinase (CK)

- Thus an increase in serum CK activity indicates damage occurs to cardiac or skeletal muscle and in rare cases to brain.
- A subsequent increase indicates an extension of the infarction.

1 Serum Creatine kinase

- After a small MI, serum CK_2 (MB) may become elevated even though the total serum CK remains within normal limits.
- Total Creatine kinase (CK) activities rise rapidly (after 4-6 hours), peaking (highest level) at 18 – 24 h, returning to normal within 2-3 days.
- The maximum rise in patients, in severe cases, may rich 10 – 20 fold of the upper limit of normal.
- CK level is directly proportional to the infraction size.



Relative levels of myocardial indicative enzymes & proteins

1 Serum Creatine kinase

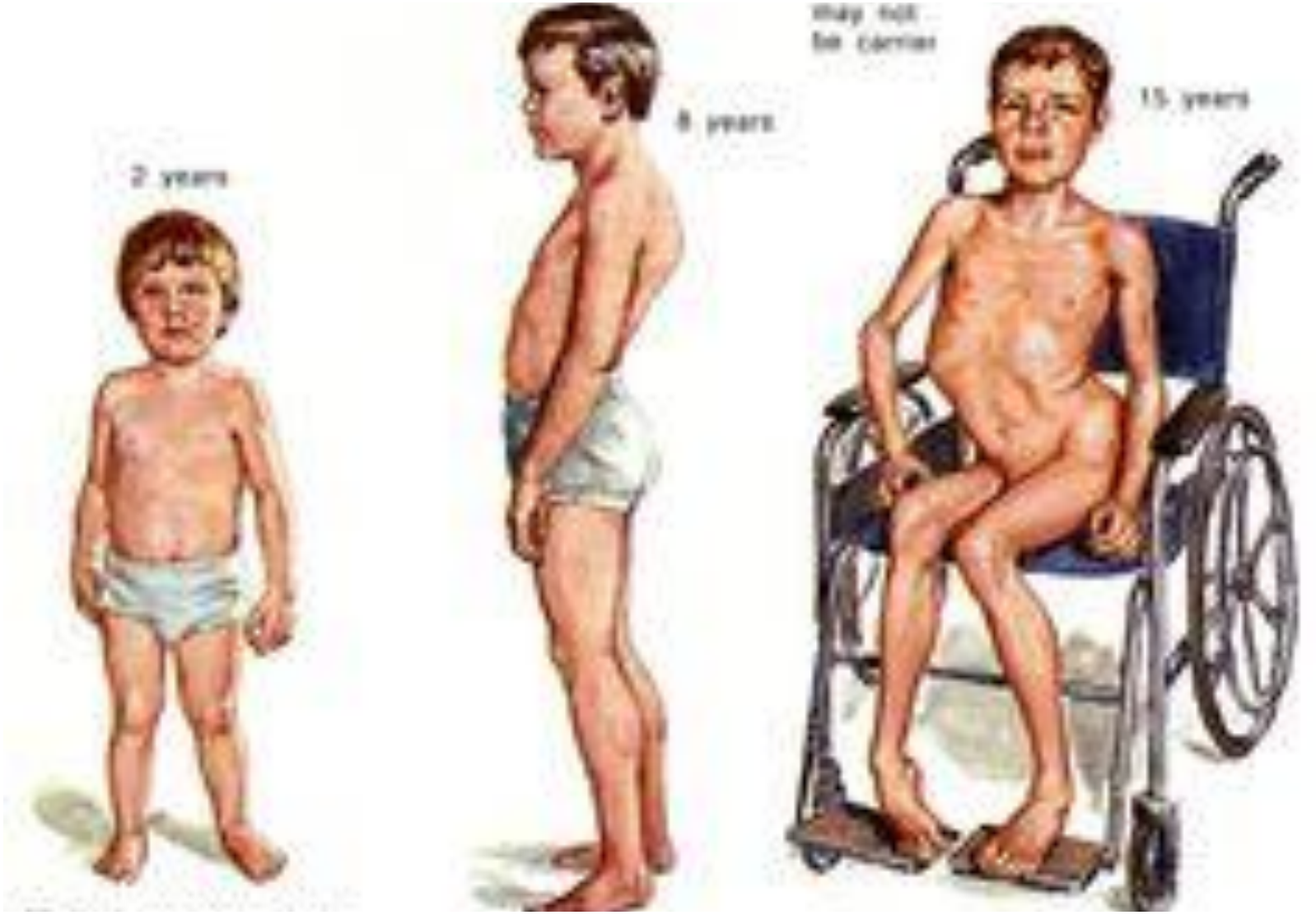
- **Physiological rise of CK:**

1. Sever muscular exercise.
2. Muscle cramps.
3. Repeated muscular injections causes transient CK rise for 2-4 days.

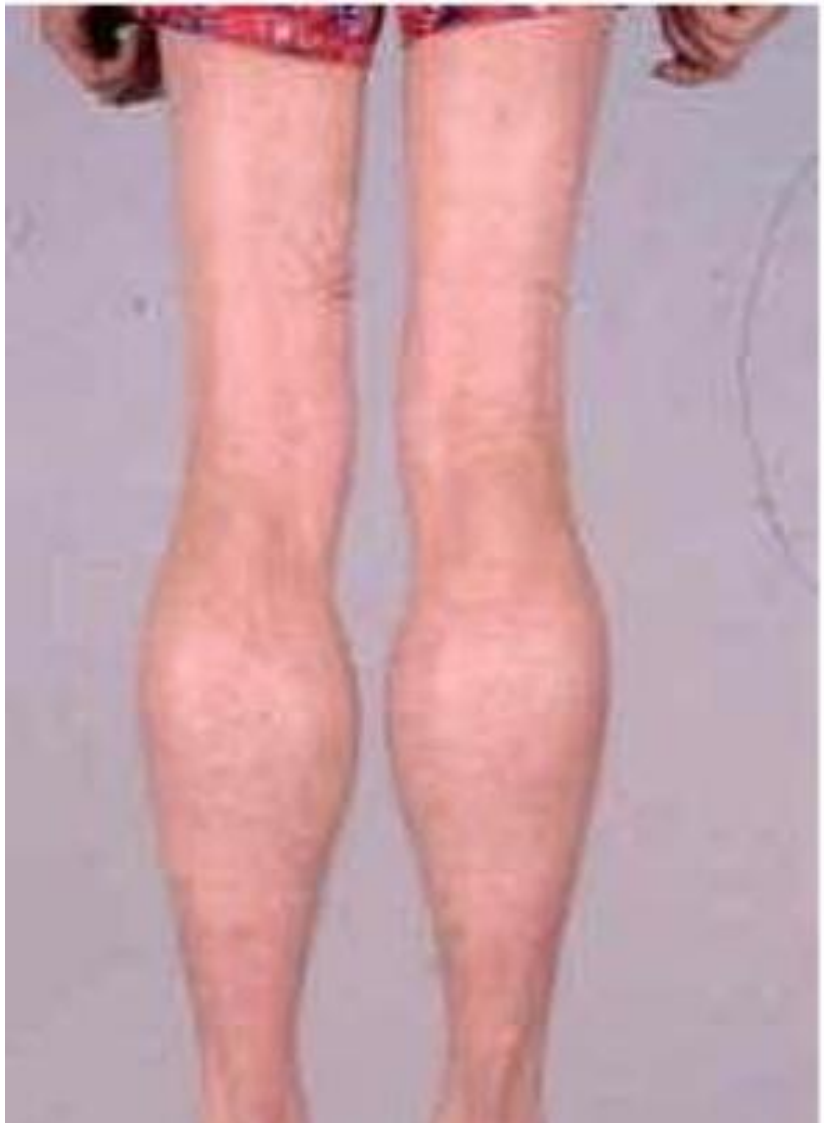
1 Serum Creatine kinase

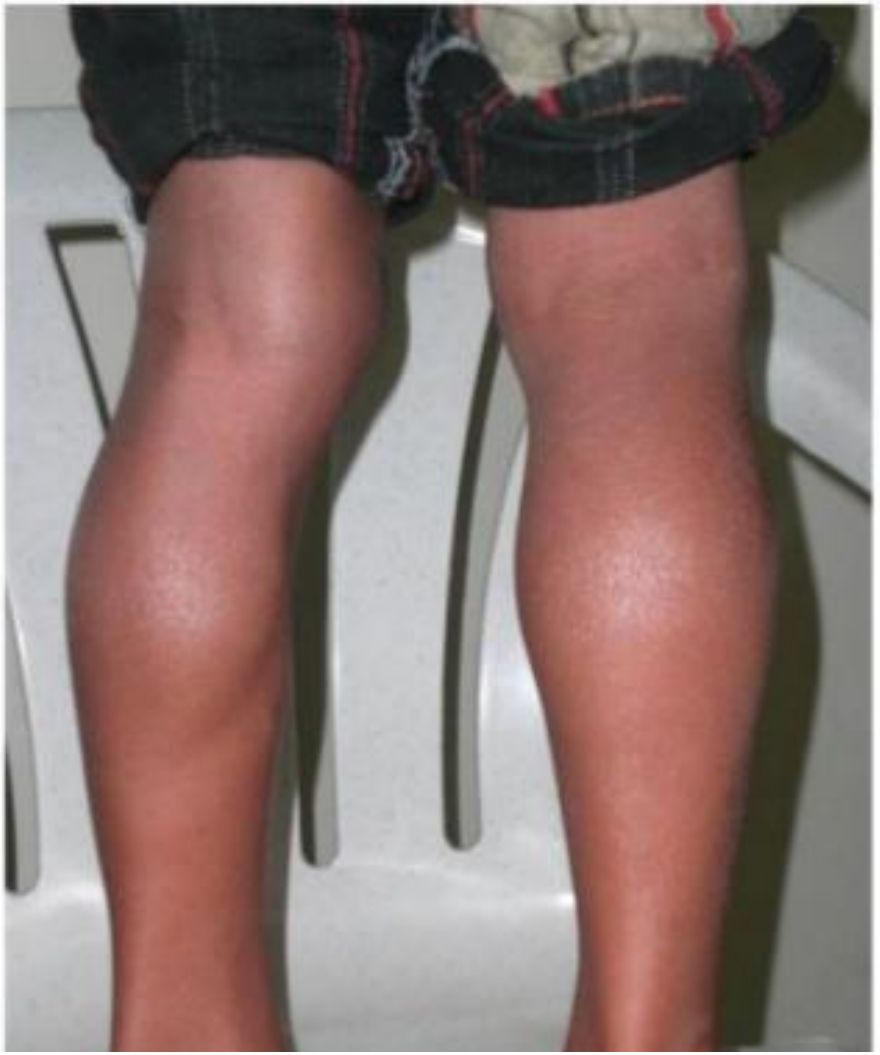
- **Pathological rise of CK:**

1. Parasitic infection caused by trichinosis (مرض دودة الخنزير).
2. Convulsions and muscle spasms.
3. Duchenne's muscular dystrophy Caused by mutation in the gene of dystrophin protein.



Duchenne's Muscular Dystrophy





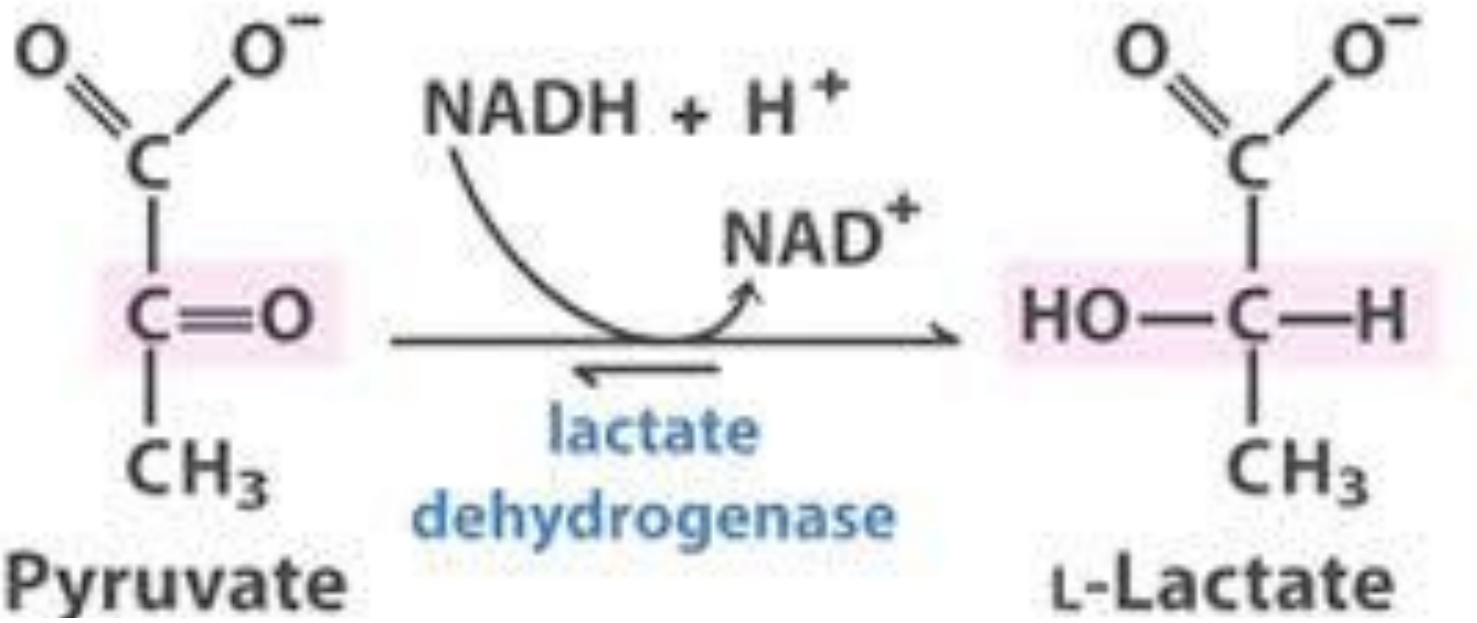
Duchenne's Muscular Dystrophy

2 Serum Lactate Dehydrogenase (LDH)

- LDH is present in all organ cells in human.
- LDH is present in high levels in cardiac & skeletal muscles, liver, kidney & red blood cells.
- In MI, the increase in serum LDH activity begins within 6-12 h and reaching a maximum (peaking) at about 48 h.

2

Serum Lactate Dehydrogenase (LDH)



$$\text{Pyruvate} + \text{NADH} \xrightarrow{\text{LDH}} \text{Lactate} + \text{NAD}^+$$

2 Serum Lactate Dehydrogenase (LDH)

Lactate DH in Heart & Muscles

Heart (H_4)

LD_1

H	H
H	H

Muscle (M_4)

LD_5

M	M
M	M

Lactate DH in different tissues

H_3M

LD_2

H	H
H	M

H_2M_2

LD_3

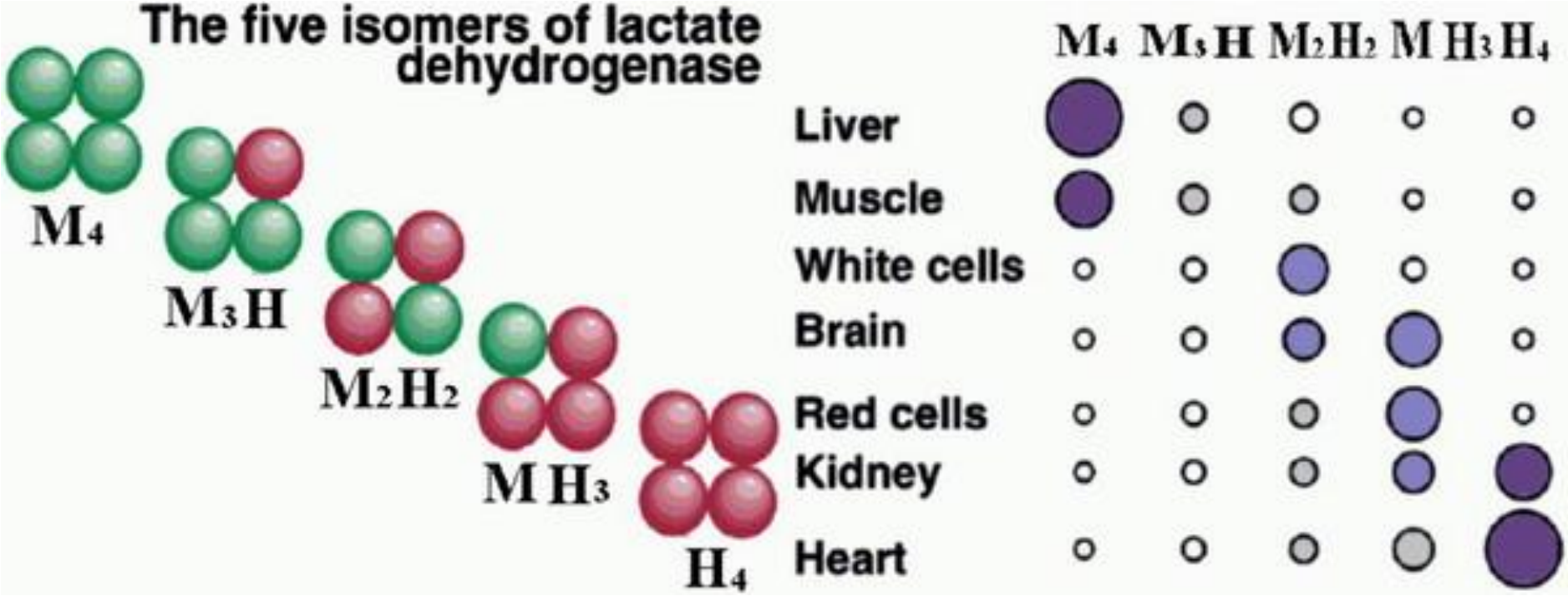
H	H
M	M

HM_3

LD_4

H	M
M	M

Distribution of different forms of LDH



- In MI the increase is mostly in LDH1 (H_4), while LDH2 may be decreased, with unchanged total LDH.

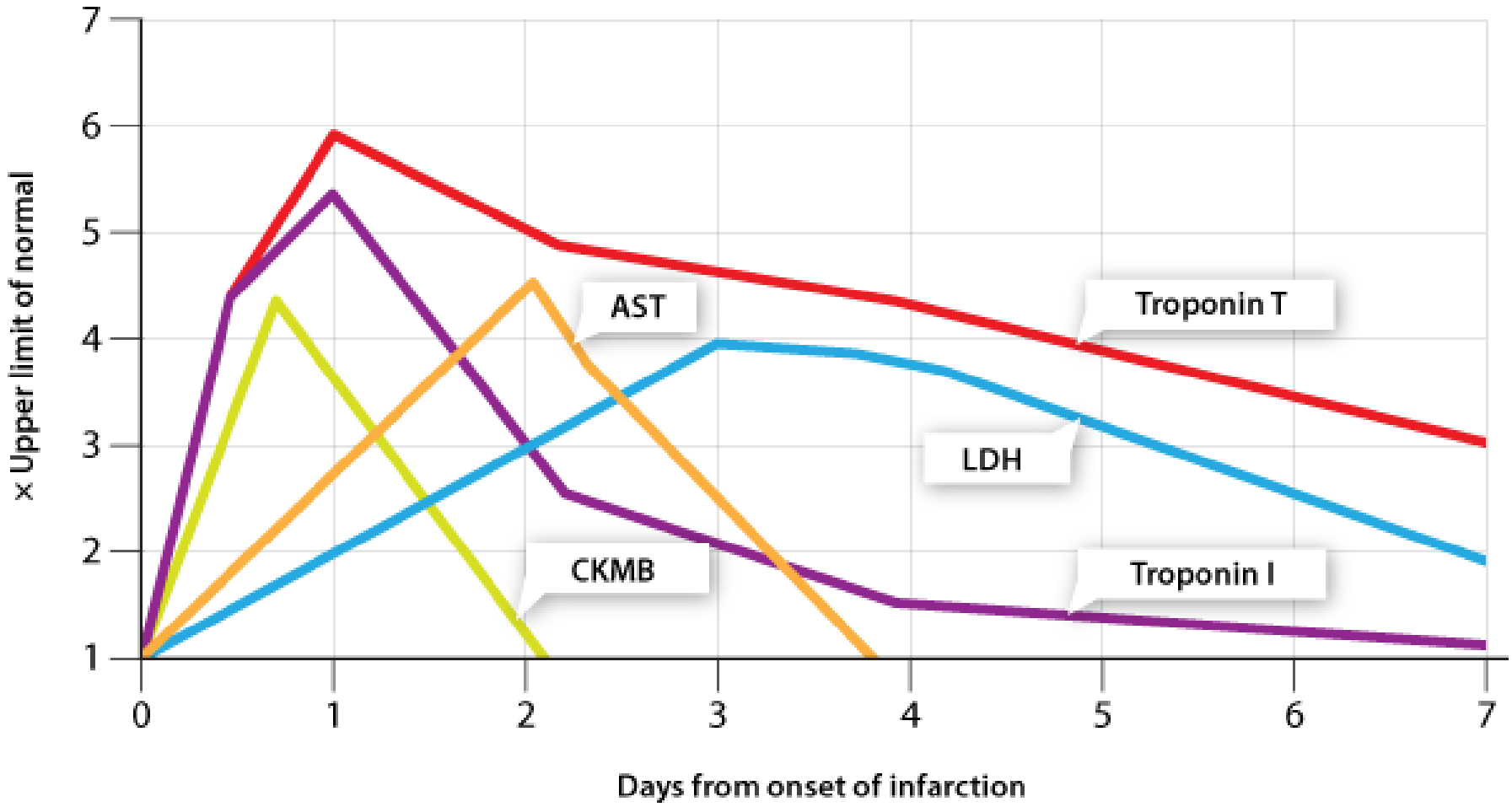
3

Serum Aspartate Aminotransferase (AST)

- AST release is not specific to MI, but is also found in many acute pathologies affecting liver and skeletal muscle.
- The enzyme alanine aminotransferase (ALT) is found in high concentration in liver rather than muscle, and a normal ALT in the face of a raised AST confirms that liver pathology is not contributing to the raised enzyme activities.

CLINICAL SIGNIFICANCE OF PLASMA ENZYME CONCENTRATIONS

SERUM ENZYME	MAJOR DIAGNOSTI C USE
Glutamic oxaloacetic transaminase (SGOT) (AST)	Myocardial Infarction
Glutamic pyruvic transaminase (SGPT) (ALT)	Infectious Hepatitis


7
6
5
4
3
2
1
x Upper limit of normal
AST
Troponin T
LDH
CKMB
Troponin I
0
1
2
3
4
5
6
7
Days from onset of infarction

AST and LDH

4

Proteins as Biochemical Markers in diagnosis of Myocardial Infarction

- Three proteins measured in serum are useful in early diagnosis and follow up of MI:

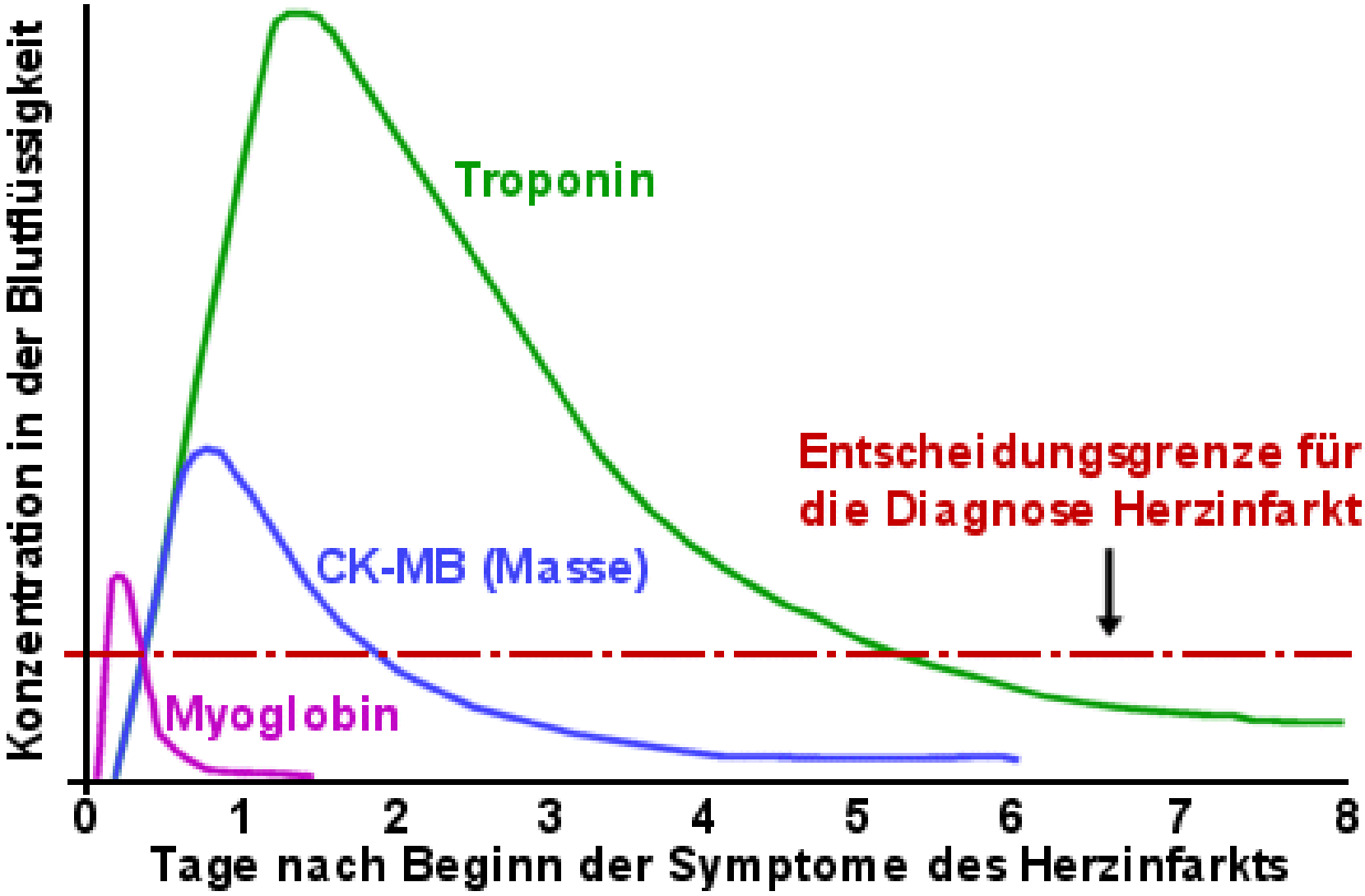
  A. Serum Myoglobin (Mb).

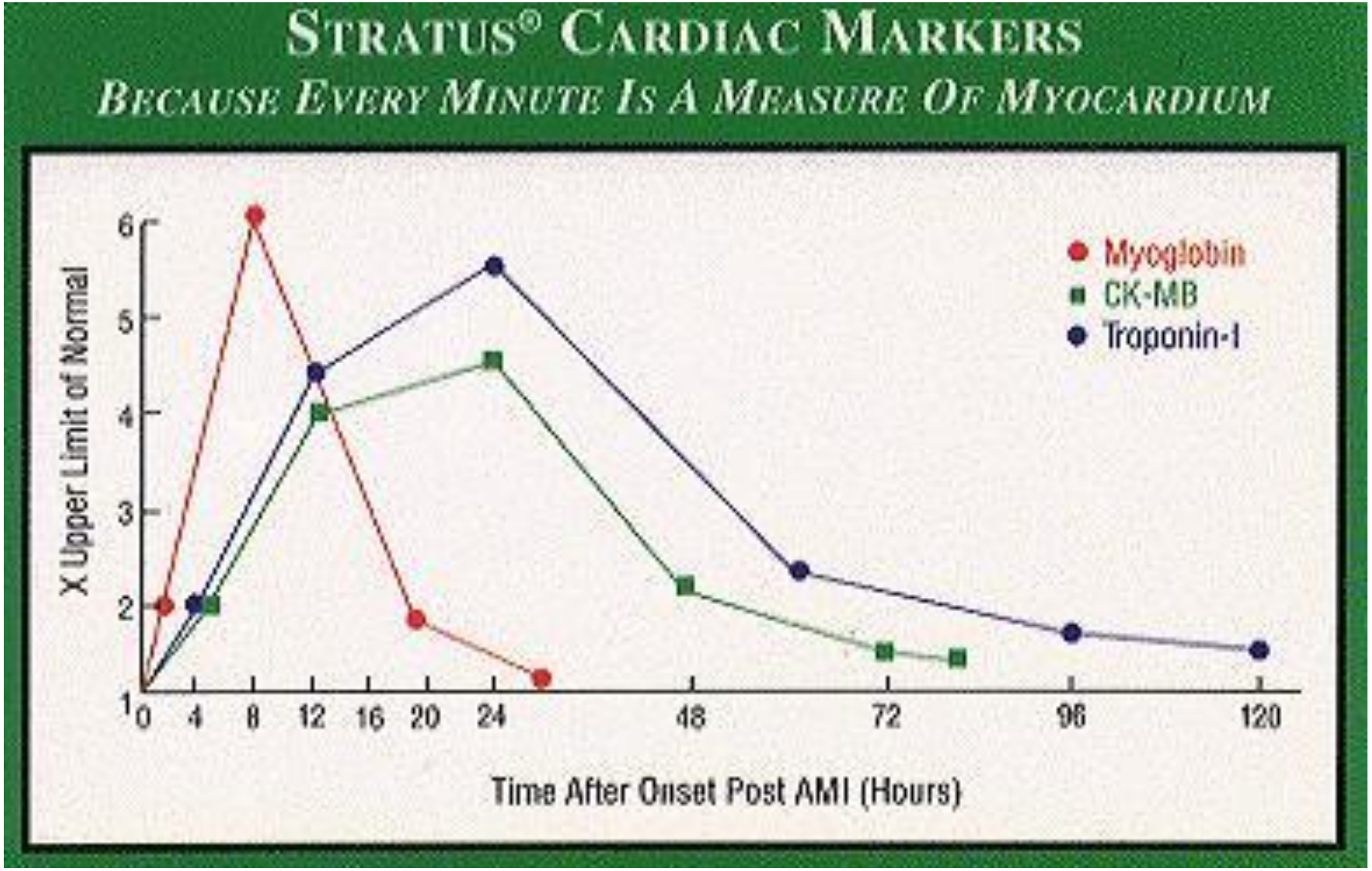
  B. Serum Troponin Complex.

  C. Fatty Acid Binding Proteins (FABP).

A. Serum Myoglobin (Mb)

- Mb is the oxygen-binding protein of cardiac and skeletal muscles.
- Mb is a monomer with low molecular weight. Its molecular weight is about one-fourth that of Hb.
- Mb small size makes it rapidly released marker in myocardial cell damage and is considered as the earliest marker of cardiac damage.
- However, myoglobin is rapidly cleared from blood within about 18 – 24 h.


Konzentration in der Blutflüssigkeit
Troponin
Entscheidungsgrenze für die Diagnose Herzinfarkt
CK-MB (Masse)
Myoglobin
0
1
2
3
4
5
6
7
8
Tage nach Beginn der Symptome des Herzinfarkts



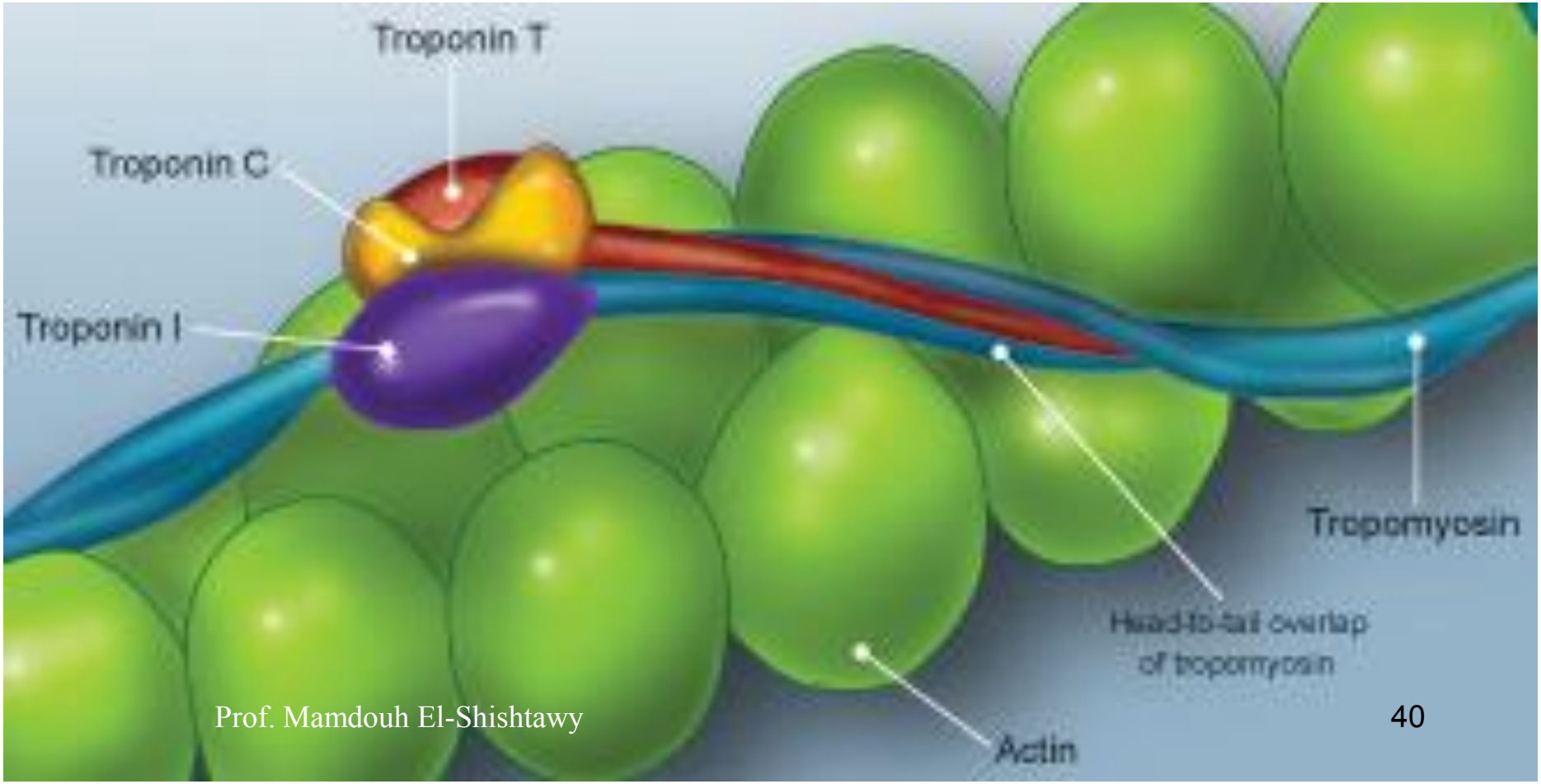
Relative levels of myocardial Creatine kinase2, Myoglobin & Troponin

A. Serum Myoglobin (Mb)

- **Skeletal muscle damage, as in trauma and strenuous exercise, also cause increase in Mb.**

B. Serum Troponin Complex

- Troponin is responsible for contraction of skeletal and cardiac muscles, but not in smooth muscle.

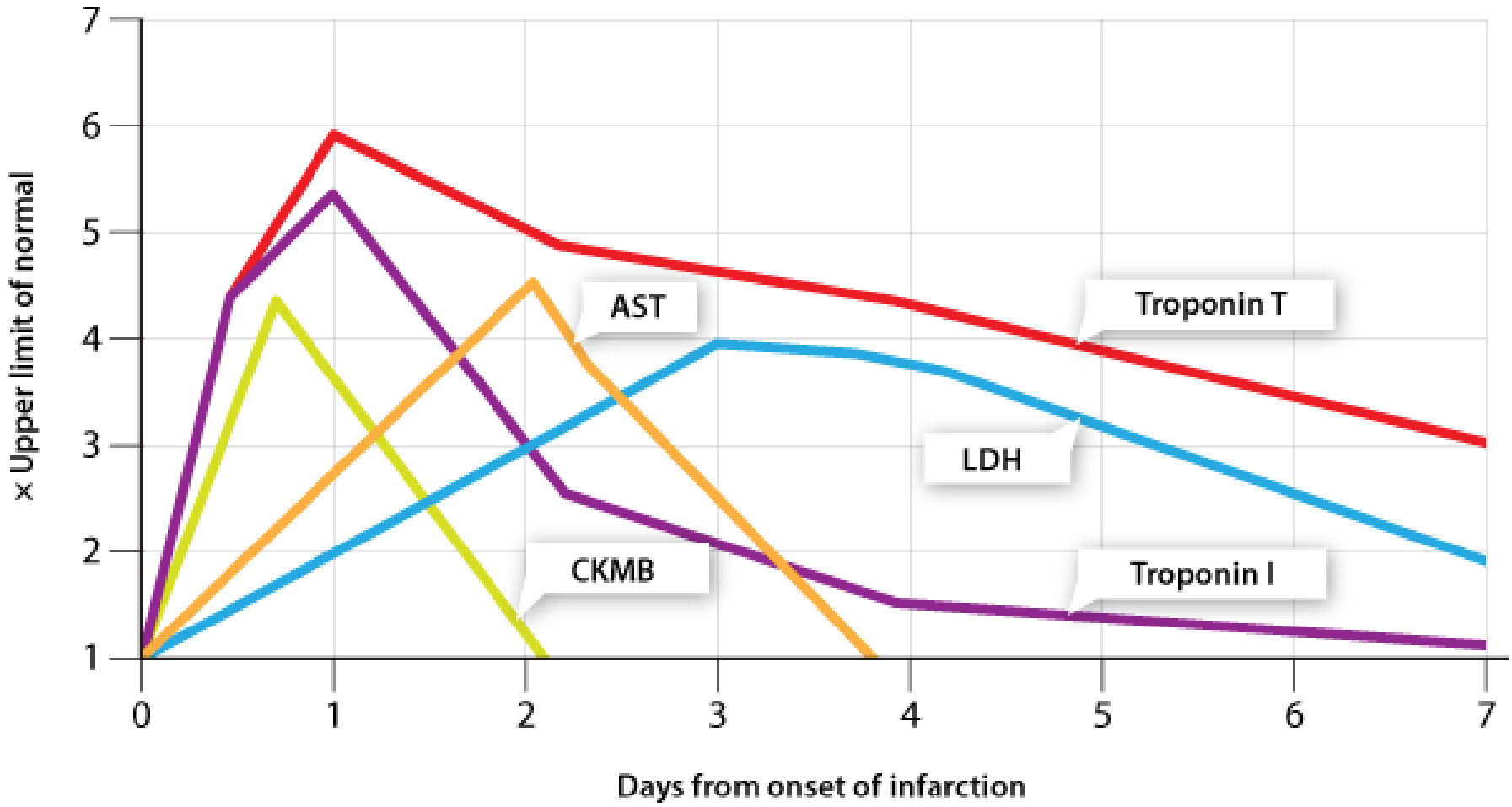


B. Serum Troponin Complex

- Troponin complex is unique to striated muscle and consists of three polypeptides:
  1. Troponin T (TpT).
  2. Troponin I (TpI).
  3. Troponin C (TpC).

B. Serum Troponin Complex

- Cardiac TpI & TpT are determined by a monoclonal antibodies assay.
- These antibodies are specific enough to interact with TpI & TpT of cardiac muscle but not of skeletal muscle.
- TpC has no cardiac-specific structure.

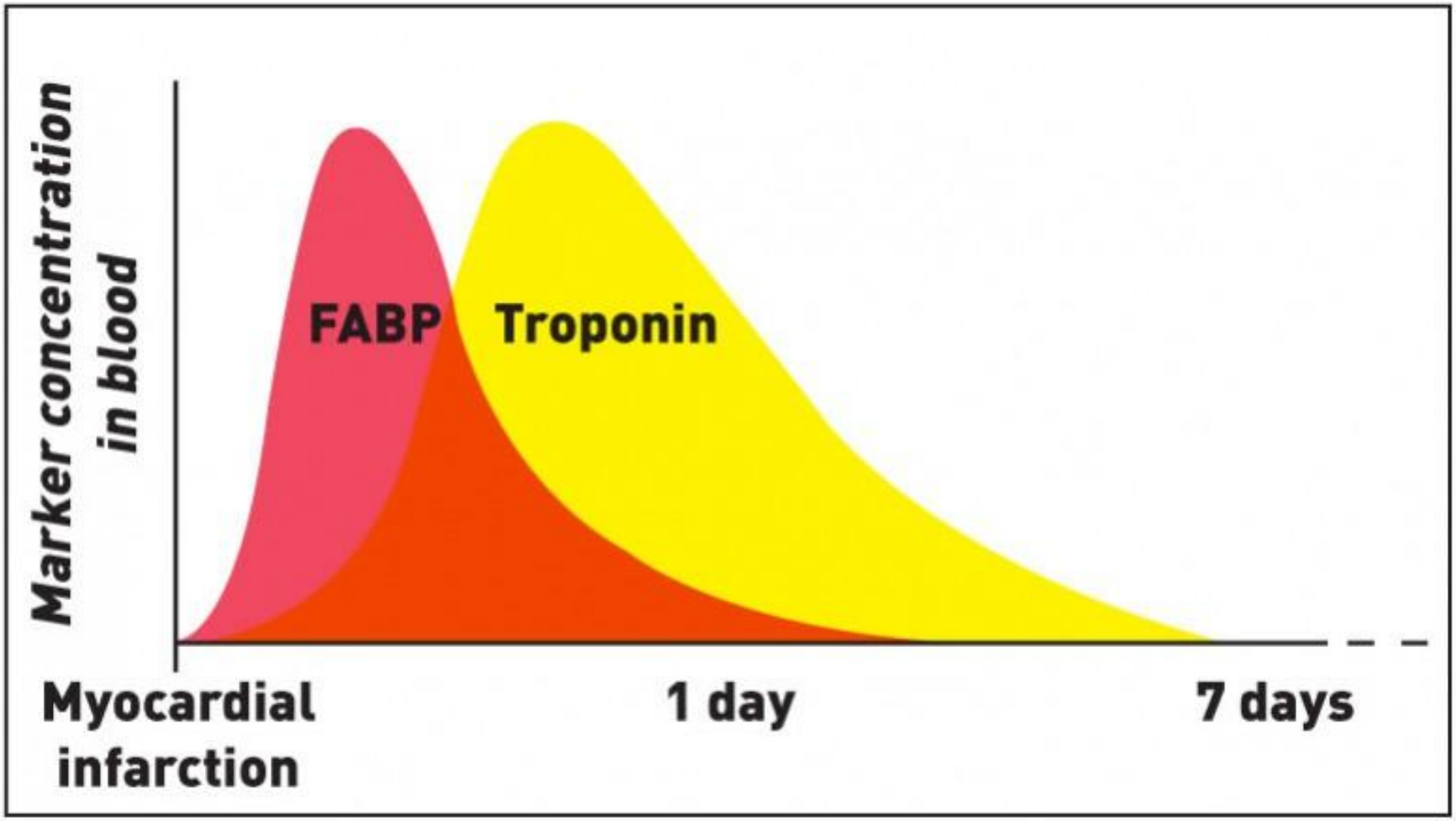


Troponin T and Troponin I

B. Serum Troponin Complex

- A negative troponin result is an appropriate "rule out" test for MI.
- However, a positive result for troponin, is significant, indicating myocardial damage.
- In the presence of typical symptoms it is strongly predictive of MI even if there are no ECG changes.

C. Fatty acid binding protein (FABP)



Fatty acid binding protein & Troponine

Characteristics of plasma biomarkers for acute myocardial infarction (AMI)

Marker protein الأقزام الذكية	Molecular mass (kD)	Elevation in plasma after AMI (h)	Peak plasma concentration (h)	Normalisation of plasma level* (days)
FABP "smart dwarf"	14.5	1 – 2	6 – 12	1 – 1.5
Myoglobin	17.8	2 – 3	6 – 12	1 – 2
Cardiac troponin I	22.5	3 – 8	12 – 24	7 – 10
Cardiac troponin T	37.0	3 – 8	12 – 24	7 – 10
Creatine kinase MB	86	2 – 6	12 – 24	2 – 3

* Dependent on (time of) reperfusion of the occluded vessels.

Thank you